REMARKS

Claims 1-8 are pending in the instant application. Claims 1-8 have been rejected. Claims 1, 3, 5 and 7 have been canceled and subject matter of these claims has been represented in new claims 9-13. The dependency of claims 2, 4, 6 and 8 has been amended to reflect the cancellation of claim 1, 3, 5 and 7 and addition of the new claims. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Rejection of Claims 1, 3, 5 and 7 under 35 U.S.C. § 112, second paragraph

Claims 1, 3, 5 and 7 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner suggests that the claims are confusing because the property of "binding affinity" is interchanged between the drug and receptor. Thus, Applicant has canceled claims 1, 3, 5 and 7 and represented subject matter claimed therein in new claims 9-13 which are drawn to prodrug complexes, immobilized prodrug complexes and methods of using

prodrug complexes comprising a selected synthetic receptor and a selected drug that binds to the synthetic receptor with lower affinity than to the drug's pathophysiologic receptor so that the selected drug preferentially binds to the pathophysiologic receptor with no loss of efficacy of the selected drug in accordance with the Examiner's suggestions. The dependency of claims 2, 4, 6 and 8 was also amended in light of the cancellation of claims 1, 3, 5 and 7 and the addition of these new claims. Withdrawal of this rejection is respectfully requested in light of these amendments.

II. Rejection of Claims 1-8 under 35 U.S.C. § 102(b) and 35 U.S.C. § 103(a)

Claims 1-8 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Morgan, Jr. et al. (U.S. Patent 5,252,713). The Examiner suggests that this patent reads on drug/carrier complexes and methods of administering a drug via these complexes wherein a drug binds non-covalently to a polymeric carrier to form a prodrug complex that is capable of allowing drug dissociation from the polymeric carrier such that the drug retains its ability to bind to a site on or within a target cell. Further, the Examiner suggests that a biologic structure, such as an antibody,

may be coupled to this complex and the carriers may bind more than one drug.

Claims 1-8 have also been rejected under 35 U.S.C. § 103(a) as being unpatentable over Morgan, Jr. et al. ('713). The Examiner suggests that the statement in the '713 patent that "drug activity also is preserved *in vivo* after administration of the conjugate to a human or mammalian host" teaches that the drug's affinity for the polymeric receptor is less than that for its pathologic receptor. Thus, the Examiner suggests that it would have been obvious to one skilled in the art at the time the invention was made to deliver a drug via a prodrug complex where the drug is bound to a polymeric carrier such that the drug would not dissociate during *in vivo* administration, but would maintain its activity by preferentially binding to its pathophysiologic receptor over the polymeric carrier with the expected result of reducing the drug's toxicity.

Applicant respectfully traverses these rejections.

It is respectfully pointed out that the polymeric carriers taught be Morgan, Jr. et al. are exclusively polypeptides. See specifically the first phrase of the Abstract; col. 3, lines 57-60; col. 7, lines 6-8, 13-38, 39-44, 45-58 and 59 bridging to col. 8, line 4; col. 8, lines 64-67; col. 9, lines 15-22 and 37-40; col. 10, lines 1-8, col. 11, lines 31-32 and col. 13, lines 6-7.

Further, the polymeric carriers described by Morgan, Jr. et al. must be derived from or identified from naturally occurring drug-binding proteins. See specifically the final sentence of the Abstract; col. 2, lines 29-31, 43-44, and 51-52; col. 3, lines 5-7; col. 4, lines 8-12 and 36-41; col. 9, lines 23-26, 55-58 and 64-66 and col. 11, lines 5-8 and 64-67.

In contrast, the synthetic receptors of the present invention include not only peptides, but also nucleic acids, antibody mimics (also referred to as molecular imprints) and synthetic polymers comprising nucleotides, carbohydrates and nonbiologic monomers. As taught in the instant specification at page 10, lines 11-16, and page 12, lines 14-18, the classes of molecules from which synthetic receptors of the present invention are selected include not only peptides but also antibodies and engineered antibodies, oligonucleotides, oligosaccharides, organic polymers such as polyhydroxyalkanoates, polyphenols, polyphosphates and polysulfates, and derivatives, analogs or combinations thereof and linear, branched and cyclized biopolymers comprising nucleotides, amino acids, saccharrides, fatty acids, phenols, phosphates, sulfates and/or other organic monomers. There is absolutely no teaching or suggestion in Morgan, Jr. et al. of a carrier comprising one of these other molecules.

Morgan, Jr. et al. also fail to teach or suggest peptide-based synthetic receptors (referred to in Morgan, Jr. et al. as polymeric carriers) selected for their ability to specifically bind a drug for which naturally occurring drug binding proteins are unknown, such as antibodies, antibody fragments, engineered antibodies, antibody mimics including molecular imprints, molecular recognition units or peptides or proteins selected from sequence or shape libraries such as combinatorial libraries or stochastic libraries, all of which are taught in the instant application and encompassed by the instant claims via the term "synthetic receptor". See, for example, page 9, line 28, through page 10, line 11, of the instant specification.

As taught throughout the specification, it is this ability to screen and identify multiple synthetic receptors for production of prodrug complexes of the instant invention which permits an array of compositional permutations from which to select and optimize specific embodiments for different clinical indications, drug classes, target distribution and pharmacokinetic objectives.

Accordingly, in an earnest effort to distinguish embodiments of the instant invention which are neither taught nor suggested by Morgan, Jr. et al., new claims 9-12 make clear that the synthetic receptor of the prodrug complex or at least one synthetic receptor

of the multi-prodrug complex is not a polypeptide derived from a naturally occurring protein to which the drug binds. Further, new claim 13 makes clear that prodrug complexes comprising a selected drug and a selected synthetic receptor can be immobilized via attachment to a biologic or biocompatible structure. No where do Morgan, Jr. et al. teach or suggest immobilization of their polymeric carrier. Instead, Morgan, Jr. et al. teach conjugation of the polymeric carrier to a targeting antibody or targeting protein to form an immunoconjugate. See specifically col. 2, lines 23-26 and 36-38; col. 4, lines 36-41; col. 9, lines 17-22; col. 10, lines 9-12 and 52-55; col. 12, lines 17-64; and the Abstract of Morgan, Jr. et al. However, conjugation of a polymeric carrier to a targeting antibody or protein known to be soluble (see col. 12, lines 24-64) does no result in an immobilized prodrug complex. Support for immobilized prodrug complexes of claim 13 can be found throughout the specification and in particular at page 5, lines 26-32; page 5, line 33, through page 6, line 24; page 10, line 26, through page 11, line 4; page 11, line 37, through page 12, line 10; page 13, line 26 through page 14, line 2; page 19, lines 3-13; and in the Examples described at pages 19-21.

The prodrug complexes as now claimed in claims 9-13 are clearly different from the complexes taught by Morgan, Jr. et al.

Thus, this reference neither anticipates nor renders obvious the instant invention. Withdrawal of these rejections is therefore respectfully requested.

III. Conclusion

Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

Jane Massey Licata
Registration No. 32,257

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Law Offices of
JANE MASSEY LICATA
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515